Saturation parameters influence on SAFARI performance

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Introduction: Amide proton transfer (APT) imaging is one of the most developed chemical exchange saturation transfer (CEST) applications. It is promising as an indicator of tissue pH[1] and a marker for brain tumors[2]. An APT imaging method using saturation with frequency alternating RF irradiation (SAFARI) was recently reported.[3-5] It can potentially remove direct water saturation without the need for additional B_0 correction and improve robustness to magnetization transfer (MT) asymmetry. The overarching purpose of this study is to expand previous work[3-5] and evaluate SAFARI performance under different experimental conditions: internal (exchange rate, MT rate, agent concentration, etc.) and external (RF shape, power, homogeneity, etc.). Here we predominantly focus on the second, and study the dependence of SAFARI on pulsed RF saturation parameters as well as the effectiveness of parallel interleave transmit (pTX)[6] compared to standard single transmit (sTX). The studies provide insights for further sequence optimization to be used in various applications other than APT.

Methods: SAFARI uses RF irradiation: (i) on-resonance with the solute group at ω_+, (ii) off-resonance at ω_- ($\omega_-=-\omega_+$), and (iii) at ω_+ and ω_- simultaneously[3,5]. The SAFARI effect is quantified by a magnetization transfer ratio (MTR) defined as $MTR_{SAFARI}=[S(\omega_-)+S(\omega_+)-2S(\omega_\pm)]/S_0$ compared with the standard analysis using $MTR_{asym}=[S(\omega_-)-S(\omega_+)]/S_0$. Simulations were performed in Matlab 8.0 (The Mathworks, Natick, MA). The total saturation time, duration of each pulse and the interpulse delay are denoted as τ_s, τ_p and τ_d respectively. The effects of the saturation power and τ_d on MTRs were studied under three regimes: (i) the amplitude of each pulse, $\omega_{1,max}$, constant or (ii) the average saturation power[7], $B_{1,pow}$, constant or (iii) the average saturation field[7], $B_{1,field}$, constant, with: $B_{1,pow}=\sqrt{\int_0^{\tau_p+\tau_d} B_1^2 dt/(\tau_p+\tau_d)}$ and $B_{1,field}=\int_0^{\tau_p+\tau_d} B_1^2 dt/(\tau_p+\tau_d)$.

A two-pool model was used to describe the proton exchange between bulk water (pool A) and the CEST agent (pool B). The simulation parameters were M_{0B}/M_{0A}=0.008 for concentration, T_{1A}=1.5 s, T_{2A}=0.8 s, T_{1B}=0.6 s, T_{2B}=33 ms for relaxation, Δ_{CS}=3.5 ppm for chemical shift difference and C_{ba}=30, 3000 Hz for exchange rates. Iopamidol (Isovue-300, Bracco Imaging) phantoms with pH equal to 6.0, 6.5, 7.0, 7.5 and 8.0 were prepared. All experiments were performed at a 3T Achieva scanner at room temperature. APT and SAFARI sequences utilizing either sTX or pTX were used and compared. RF pulses ranged from -10 ppm to 10 ppm with τ_s=2.5 s and τ_p=49.5 ms. Images were acquired using FFE or TSE, FOV=250×250 mm, image matrix=256×256, slice thickness=10 mm. T_1 and T_2 were measured using inversion recovery and multi-echo SE. The exchange rate was calculated by fitting the Z-spectrum.

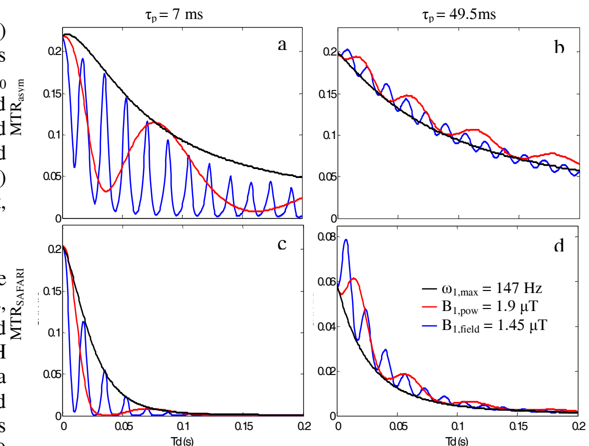

Fig. 1 Influence of τ_d with post-pulse crushers.

Results and Discussion: The influence of τ_d is shown in Fig. 1. Overall, the shortest τ_d leads to the maximum MTR_{asym} and MTR_{SAFARI}. For short τ_p, there is no substantial difference between the maximum values of MTR's. However the difference becomes substantial for long τ_p with a remarkable loss of SAFARI effect. As τ_d increases, both MTR_{asym} and MTR_{SAFARI} decrease, however MTR_{SAFARI} decreases much faster than MTR_{asym}. We investigated the three regimes described above. (i) When keeping $\omega_{1,max}$ constant, increasing τ_d leads to decreasing $B_{1,pow}$ and $B_{1,field}$. Thus MTR's decrease due to insufficient saturation of solute protons (Fig. 1, Black). In the regimes (ii) and (iii), increasing τ_d leads to vanishing MTR_{asym} and MTR_{SAFARI}. We hypothesize that the CEST effect decrease in these regimes (Fig. 1, Red and Blue) is due to relaxation influence during τ_d as shown in Eq. 1: steady-state under pulsed irradiation for pool B $M_z^B=\frac{M_0^B(1-e^{-\tau_d/T_1})}{1-e^{-\tau_d/T_1}\cos FA}$ (Eq.1).

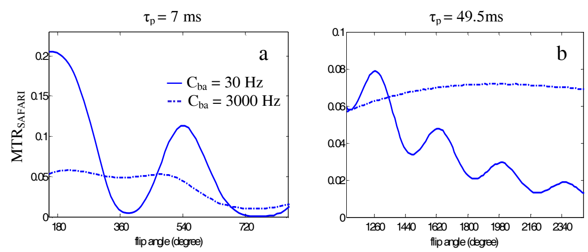

Fig. 2 MTR_{SAFARI} for varying FA with post-pulse crushers.

The influence of the flip angle (FA) for a constant $B_{1,field}$ is shown in Fig. 2. Interestingly, the MTR_{asym} (not shown) and MTR_{SAFARI} vs FA show oscillations, with maximum values around FA=180º+360º×N (N = 0,1,2,…). Similar phenomenon was observed in Ref. 7 and explained by solute rotation effects[7]. Another perspective can be seen from Eq.1 (Ernst angle): for the pulsed saturation at steady-state, M_z is always minimal with FA=180º. As Fig. 2 indicates, the oscillations are gradually weakened as τ_p and exchange rate C_{ba} increase. In addition, the performance of SAFARI is influenced by C_{ba}. If C_{ba} is large (i.e. the exchange too fast), SAFARI method becomes less efficient.[4] Similar influence of FA on MTRs for a constant $B_{1,pow}$ was seen.

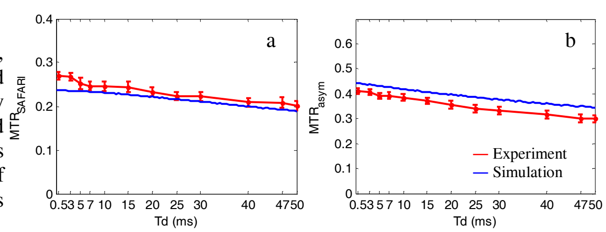

Fig. 3 Influence of τ_d. Keeping $B_{1,field}$ = 1.89 μT.

The experimental and simulation results for phantom with pH=7.5 are shown in Fig. 3. The measured parameters for the phantom were: M_{0B}/M_{0A}=0.014, T_1=3 s, T_2=2.4s, C_{ba}=2750 Hz and Δ_{CS} =510 Hz. These parameters were used as simulation parameters. As Fig.3 indicates, the simulation is in good agreement with the experiments. The exchange rate is fairly high, leading to less efficient SAFARI performance. At the same time it is less dependent on the power, thus indicating successful application at lower specific absorption rate (SAR), for both SAFARI and APT schemes. In the phantom experiment so far, there were no significant differences between sTX and pTX (not shown here).

Conclusion: This study evaluated the influences of different parameters on the SAFARI imaging performance. Both APT and SAFARI effects decrease with increasing interpulse delay. However, the amount of decrease is dependent on RF parameters as well as the exchange rate. Moreover, SAFARI is more sensitive to the choice of individual pulse length with the optimal performance at short interpulse delay. In all cases, pulse flip angles of 180º+360ºN lead to the most efficient saturation. In some systems, efficient saturation can be achieved with increased interpulse delay, thus lowering SAR without compromising CEST effect. Work is underway to apply SAFARI for hydroxyl protons detection as well as study the influence of various MT parameters.

References: [1] Zhou J, et al. Nat Med.2003;9(8):1085-1090. [2] Zhou J, et al. MRM.2003;50(6):1120-1126. [3] Scheidegger R, et al. MRM.2011;66(5):1275-1285. [4] Scheidegger R, et al. Proc. ISMRM.2010;18:2987. [5] Scheidegger R, et al. Proc. ISMRM.2011;19:2769. [6] Keupp J, et al. Proc. ISMRM.2011;19: 10. [7] Zu Z, et al. MRM. 2011; 66(4): 1100-1108.